## REMARKS AND DISCUSSION

Applicants have canceled claims 1-40 and have added independent claim 72 and dependent claims 73-106, independent claim 107 and dependent claims 108-140 and independent claim 141. Claims 72 and 107 are directed to the same subject matter as independent claim 1 and claim 141 is directed to the same subject matter as independent claim 40. The newly added claims find support in the Specification at pages 8-15, in claims 1-40 and in the Summary of the Invention.

In view of the following discussion, Applicants submit that claims 72-141 are directed to statutory subject matter under the provisions of 35 U.S.C. §101, comply with the requirements of 35 U.S.C. §112, and are not anticipated under the provisions of 35 U.S.C. §102. Thus, Applicants believe that claims 72-141 are now in condition for allowance.

## I.     OATH AND DECLARATION

A new oath and declaration in compliance with 37 CFR 1.67(a) is submitted herewith. On the new oath, the fling date of the provisional application has been corrected.

## II     INFORMATION DISCLOSURE STATEMENT

An Information Disclosure Statement is submitted herewith to provide the references which correspond to referenced documents AI, AN, AO, AP, AQ, AR, AT, AY, AGG and ANN.

## III.   REJECTION OF CLAIMS 1-40 UNDER 35 U.S.C. § 101

The Examiner has rejected claims 1-40 under 35 U.S.C. §101 as being directed to non-statutory subject matter.

Claims 1-40 have been canceled, and claims 72-141 have been added and are believed to be directed to statutory subject matter under the provisions of 35 U.S.C. §101. Applicants submit that claims 72-141 fully satisfy the requirements of 35 U.S.C. §101 and are patentable thereunder.

## IV.   REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner has rejected claims 1-40 under 35 U.S.C. §112, first paragraph.

Claims 1-40 have been canceled, and claims 72-141 have been added. Applicants submit that claims 72-141 satisfy the requirements of 35 U.S.C. §112, first paragraph, and are patentable thereunder

## V.   REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected claims 1- 38 under 35 U.S.C. §112, second paragraph.

Claims 1-38 have been canceled, and claims 72 –141 have been added. Applicants submit that claims 72-141 satisfy the requirements of 35 U.S.C. §112, second paragraph, and are patentable thereunder

## VI.   REJECTIONS UNDER 35 U.S.C. §102(b)

The Examiner has rejected claims 1, 4, 5, 11-18, 21-28, 31, 34 and 39 under 35 U.S.C. § 102(b) as being anticipated by Nielsen et al (Protein Engineering, 12(1):3-9, 1999). Claims 1, 4, 5, 11-18, 21-28, 31, 34 and 39 have been canceled, and claims 72-141 have been added. Applicants respectfully disagree with the rejection as it applies

to claims 72 - 141.

The Examiner is stating that Nielsen teaches a hidden Markov model for signal peptide and signal anchor prediction which is put together from combined models having different states. Each model included two or three regions and processing sites were predicted. Peptide sequences were used to develop the module and a given set of sequences is compared to the model to train and predict.

Nielsen teaches that while hidden Markov models (HMMs) are best at recognizing in an "elastic" fashion the sequential pattern in the amino acids or nucleotides, the neural networks (NNs) algorithms are better at handling sequence features correlated over a longer range. As an alternative to HMMs and NNs, to identify secretory signal peptides (SP), Nielsen teaches the use of SignalIP (Page 3, 3rd paragraph). SignalIP Is an NN-based method which combine two different NNs, one that has been trained to classify each residue, in the sequences as either belonging or not belonging to an SP (S-score), and one that has been trained only to recognize the site at the C-terminal end of the SP that is cleaved by the signal peptidase enzyme after targeting (C-score). Cleavage-site prediction performance Is significantly enhanced by penalizing C-score peaks that are far away from the transition region between the SP and mature polypeptide Identified by the S-score. This is formalized by the Y-score, a geometric average of the C-score and a numerical derivative of the S-score. A prediction of the existence of an SP can be made by the maximal value of the S, C and Y scores, or the mean S score between the N-terminus and the predicted cleavage site. (Page 4, paragraphs 7 and 8).

To distinguish signal peptides (SP) from signal anchors (SA), Nielsen teaches the use of SignalIP-HMM (Page 5). Figure 2 is an illustration of SignalIP-HMM for signal peptide and signal anchor prediction. The model of SP and SA is used to predict the amino acid distribution of a single peptide sequence.

As stated by Applicants (Specification, page 11, paragraph 4), Nielsen have adapted trained profile HMMs which model just one sequence, to produce a model of a pair of sequences which fit the profile for a single signal sequence.

By contrast with Nielsen, as set forth in claims 72, 107 and 141, the model of the present invention looks for a pattern of match states or score variations across the modules and allows for the identification of biopolymer sequences using a statistical model of a set of known sequences characterized by a topological pattern of match states, with each match state represented by a module of nodes trained against a set of data objects, and compares the match states of the set of known sequences to the match states of the biopolymer sequences to identify the biopolymer sequences. By looking for a pattern of match states across the modules that fits a predetermined evolutionary match profile, the model rewards and penalizes each module differentially and thus allows for the identification of a set of biopolymer sequences.

As stated above, by teaching adapted trained profile HMMs which model just one sequence, to produce a model of a pair of sequences which fit the profile for a single signal sequence, Nielsen does not teach nor suggest the identification of a set of biopolymer sequences according to their match states by differential scoring. Thus Nielsen fails to anticipate or make obvious Applicants' invention as set forth in claims 72, 107 and 141.

Therefore, Applicants submit that independent claims 72, 107 and 141 fully satisfy the requirements of 35 U.S.C. §102 and are patentable thereunder.

Dependent claims 73-106 and 108-140 which depend from claims 72 and 107and recite additional features, are also not anticipated by the teachings of Nielsen. Therefore, the Applicants submit that dependent claims 73-106 and 108-140 fully satisfy the requirements of 35 U.S.C. §102 and are patentable thereunder.

## Conclusion

Thus, Applicants submit that all of these claims now fully satisfy the requirements of 35 U.S.C. §101, §112 and §102. Consequently, the Applicants believe that all the claims are presently in condition for allowance. Accordingly, both reconsideration of this application and its swift passage to issue are earnestly solicited.
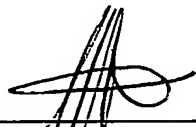
If, however, the Examiner believes that there remains unresolved issues, prior the issuance of a final action in any of the claims now pending in the application, it is

requested that the Examiner grant Applicants a telephone interview by contacting the undersigned at (732) 530-9404 so that such issues are resolved as expeditiously as possible.

If these papers are not considered timely filed by the United States Patent and Trademark Office, or if any additional fees are required, kindly charge that fee to Deposit Account No. 20-0782.

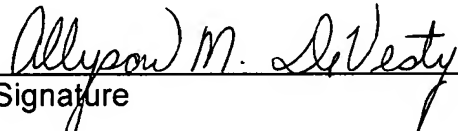Respectfully submitted,

Date: 12/12/03

Lina Genovesi
Attorney for Applicants
Reg. No. 35,154
(732) 530-9404

Moser, Patterson & Sheridan, LLP
595 Shrewsbury Avenue
Shrewsbury, New Jersey 07702

## CERTIFICATE OF MAILING UNDER 37 C.F.R. 1.8(a)

I hereby certify that this correspondence is being deposited on <u>December 12, 2003</u> with the United States Postal Service as first-class mail, with sufficient postage, in an envelope addressed to Mail Stop Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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